A Curious Case of Acute STEMI in a Young Patient; Things are Not Always What They Seem

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Abstract

**BACKGROUND:** Acute myocardial infarction (MI) is a rare occurrence in patients under 40 years of age without positive family history for coronary artery disease (CAD). Genetic conditions as inherited thrombophilia can lead to a hypercoagulable state, resulting in thromboembolic events and arterial thrombosis.

**CASE SUMMARY:** We present a case of a 35-year-old male patient who presented to the emergency room with an inferior MI after a strenuous cycling exercise. An urgent coronary angiography showed thrombotic formations in the right coronary artery without atherosclerotic plaques. Plain old balloon angioplasty and thrombus aspiration were performed, which was followed by GP IIb/IIIa inhibitor infusion and unfractionated heparin for 24 h. From past medical history, the patient had COVID-19 like symptoms 20 days before the event and had his first dose of anti-COVID vaccine 2 weeks prior. After additional testing, molecular genetic analysis results revealed the patient to be heterozygous for factor V Leiden (FVL) and homozygous for methylenetetrahydrofolate reductase C677T gene mutation. The patient was discharged on direct oral anticoagulant and antiplatelet therapy. After 1-year follow-up, he had no symptoms or recurrent cardiovascular events.

**CONCLUSION:** Inherited thrombophilia is a significant risk factor for CAD and performing genetic testing in younger patients with a cardiovascular event and plays an important role for adequate treatment and prophylaxis from recurrent complications. The use of oral anticoagulation for prophylaxis is shown to be effective in these patients. However, further studies are needed to prove their exact role and duration of treatment.

Introduction

Coronary artery disease (CAD) is the leading cause of mortality in the world population. Myocardial infarction (MI) generally occurs in the elderly and is uncommon in patients younger than 45 years [1], [2]. The etiological factors leading to MI in younger patients can be classified as atheromatous CAD, non-atheromatous CAD, hypercoagulable states, and MI related to substance abuse [3].

Inherited thrombophilia represents a wide range of genetic disorders which are characterized by an increased tendency to develop thrombotic formations. It leads to a hypercoagulable state that results in venous thromboembolic complications, as well as arterial thrombotic events such as ischemic stroke and MI [4].

Heterozygous Leiden V factor gene mutation is the most common type of inherited thrombophilia, and its prevalence is approximately 1–5% in the general population. It is an autosomal dominant genetic condition, which is caused by a single-point mutation in the factor V gene that leads to the replacement of the 506 amino acid arginine with glutamine. As a result, the activated protein C cannot bind and inactivate the mutated form of factor V, which continues to be active and increases the risk of thrombosis. It is found that Leiden factor V heterozygosity increases the risk of thrombotic events 7-folds during the lifetime, whereas homozygosity increases the risk up to 20-fold. It is generally characterized by the increased tendency to venous thromboembolic events [5].

Methylenetetrahydrofolate reductase (MTHFR) gene mutation results with the abnormal formation of the MTHFR enzyme, which catalyzes the conversion of the 5, 10-methylenetetrahydrofolate to 5-methyltetrahydrofolate. Its deficiency causes elevated serum levels of homocysteine, which is associated with CAD. There are over 20 gene polymorphisms known for the MTHFR enzyme, where C677T is among the most studied ones. Although they are associated with different health issues, C677T is found to have the strongest association with CAD [6].

COVID-19 infection has been connected to prothrombotic conditions such as acute MI in patients, especially in the 1st month of the primary infection [7], [8], [9] A recent study also demonstrated the long-term cardiovascular events post-COVID-19 infections, beyond the first 30 days after infection, building a cohort of 153,760 individuals with COVID-19 and comparing them to two sets of control cohorts. Results showed that individuals with COVID-19 were at increased risk of incident cardiovascular disease, including
thromboembolic disease, compared to the control groups [10]. The underlying mechanisms of thrombogenesis may include the direct pathogenic effect of SARS-CoV-2 on the endothelial cells and microvascular damage, increased production of inflammatory cytokines, and hypercoagulable state due to increased activation of the coagulation cascade and thrombosis [11]. Recent studies have also shown that COVID-19 increases the risk of MI, especially in the presence of risk factors including dyslipidemia, smoking, obesity, or genetic conditions as inherited thrombophilia [7].

In this case, we present a young male patient with acute MI due to inherited thrombophilia as a combination of FVL and MTHFR C677T gene mutation with a recent COVID-19 infection.

Case Report

A 35-year-old male patient presented to the emergency room with severe chest pain that started 2 h ago during a strenuous cycling exercise at a distance of 11 km. He did not have a past medical history or a family history for cardiovascular diseases. He was a nonsmoker and physically active, regularly cycling for 12–20 km per day. 1 month before hospitalization, he experienced Covid-19 like symptoms with dyspnea and anosmia, but without confirmation with a PCR test for COVID-19, while 2 weeks before admission, he has had his first anti-COVID-19 vaccine.

On physical examination, his blood pressure was 140/90 mmHg and a heart rate of 90/min. The electrocardiogram showed sinus rhythm with a heart rate of 93/min, normal heart axis, and ST segment elevation of 3mm in the inferior leads (D2, D3, aVF) (Figure 1).

An urgent coronarography was indicated which showed thrombotic formations in the proximal part of the right coronary artery, right postero-descending artery and right postero-lateral artery without atherosclerotic plaques (Figure 2). Percutaneous coronary intervention with plain old balloon angioplasty and thrombus aspiration with Export 6 catheter was performed, which was followed by a dose of GP Iib/IIa inhibitor, i.e., bolus and infusion, afterward continuing with infusion of unfractionated heparin for 24 h in addition to antiplatelet treatment (Figure 3).

The initial blood analysis showed mildly increased values of hs troponin I - 32.87 ng/mL, which increased up to 13132 ng/ml on the 2nd day of hospitalization and returned to normal values before discharge. From the additional blood work, a D-Dimer test was performed showing elevated values to 2237 ng/mL.

Transthoracic echocardiography revealed normal dimensions, systolic, and diastolic function of the left ventricle with EF-60%. There was dyskinesia on the basal segment of the inferior wall of the left ventricle.

Additional genetic tests were warranted due to the unknown cause of this event. Molecular genetic test by the method of reverse hybridization on the DNA isolated from the leukocytes of the peripheral blood showed the patient to be heterozygous for FVL and homozygous for MTHFR C677T gene mutation.

After 8 days of hospitalization, the patient was discharged in a good clinical condition with a recommendation for medical treatment including a prophylactic dose of direct oral anticoagulation and antiplatelet treatment.

After 1-year follow-up, the patient had no symptoms or recurrent cardiovascular events and was continued on prophylactic dose of NOAC.

Discussion

The prevalence of hereditary thrombophilia in the general population is rare (approximately 0.25–0.5%). Inherited thrombophilia due to a combination of Leiden factor V and MTHFR C677T gene mutation is generally associated with venous thromboembolic events, whereas their role in arterial thrombosis remains uncertain [4].

Leiden factor V gene mutation is one of the most studied variants of thrombophilia, which is generally associated with a higher risk for VTE. On the other hand, there have been published conflicting results on the role of FVL mutation in the development of CAD [12]. The past studies and meta-analysis were not conclusive or they did not show any association between the FVL gene mutation and arterial thrombotic events. The first meta-analysis that represented the role of FVL mutation in the development of MI was the meta-analysis by Ye et al. [13], where 66 155 patients and 91 307 controls were included (odds ratio [OR], 1.22; 95% CI, 1.10–1.35). In recent years, there have been many meta-analyses and case series that confirm this association [14]. In a meta-analysis of 56 studies, in which 49 reported homozygosity and heterozygosity status for FVL mutation, it was reported that FVL was found in significantly more arterial ischemic stroke cases than controls, irrespective of zygosity status [15].

There has been a reported association between MTHFR C677T gene mutation and CAD [16]. A meta-analysis of published studies on the role of FVL, prothrombin G20210A, and MTHFR C677T mutations and events of the arterial circulatory system, presented an increased risk of MI and ischemic stroke in these patients, especially at a younger age [17].

There are no established guidelines on the indication and duration of prophylactic oral anticoagulation treatment in patients with inherited thrombophilia with the first arterial thrombotic event. In published literature, there are reported studies and case series about the use of anticoagulation treatment in patients with hereditary thrombophilia after MI to prevent recurrent cardiovascular events [4]. In our case, the patient was discharged with recommendation of preventive dose of oral anticoagulation treatment and after 1-year follow–up, the patient was in a good clinical condition with no recurrent cardiovascular event or bleeding complications.

**Conclusion**

Combination of Leiden factor V and MTHFR C677T gene mutation is rare, but an important risk factor for CAD, especially in younger patients. Performing genetic testing in younger patients with the first cardiovascular event plays an important role for adequate treatment and prophylaxis from recurrent complications. COVID-19 infection can act as a trigger factor in these conditions and increase the possibility for a thrombotic event.

Although individual patient consideration is recommended, the use of oral anticoagulation for prophylaxis is shown to be safe and effective in these patients. However, further studies are needed to prove their exact role and duration of treatment.

**References**


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PMid:32595241


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